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5,6,7-Trimethoxy-2,3-dihydroinden-1-one

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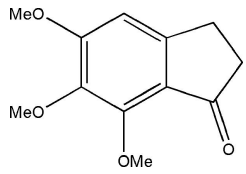
Key indicators: single-crystal X-ray study; T = 173 K; mean σ(C–C) = 0.002 Å; R factor = 0.036; wR factor = 0.099; data-to-parameter ratio = 16.8.

The bicyclic ring system of the title compound, $C_{12}H_{14}O_4$, is essentially planar. One of the methoxy groups is almost coplanar with the ring system, but the other two are considerably twisted out of its plane.

Related literature

For background literature on indanones and their biological applications, see: Andreani *et al.* (2000); Cai *et al.* (2005); De Paulis *et al.* (1981); Hanna & Lau-cam (1989); Howbert & Crowell (1990); Kwiecien *et al.* (1991); Mithofer *et al.* (2005); Omran *et al.* (2005); Pinkerton *et al.* (2005); Yamamoto *et al.* (1994).

For related literature, see: Allen (2002); Biggs *et al.* (1976); Bruno *et al.* (2004); Rambaldi *et al.* (2001).



Experimental

Crystal data

$C_{12}H_{14}O_4$
M_r = 222.23
Monoclinic, $P2_1/n$
a = 8.9319 (7) Å
b = 7.2870 (5) Å
c = 16.8250 (12) Å
β = 94.070 (6)°
V = 1092.32 (14) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 173 (2) K
0.44 × 0.36 × 0.35 mm

Data collection

Stoe IPDSII two-circle diffractometer
Absorption correction: none
13559 measured reflections
2503 independent reflections
2228 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.099
S = 1.05
2503 reflections
149 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Selected torsion angles (°).

C10—O1—C1—C6	−71.82 (13)	C12—O3—C3—C4	−1.56 (15)
C11—O2—C2—C3	80.44 (12)		

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB2386).

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supplementary materials

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5,6,7-Trimethoxy-2,3-dihydroinden-1-one

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Comment

Indanones are useful precursors in the synthesis of a variety of biologically active compounds including indacrinone (Hanna & Lau-cam, 1989), indanoyl isoleucine conjugates (Mithofer *et al.*, 2005), indanocines (Andreani *et al.*, 2000) and other medicinally important products (Pinkerton *et al.*, 2005, Yamamoto *et al.*, 1994, Briggs *et al.*, 1976). Donepezil, a 5,6-dimethoxyindanone and its derivatives, are acetyl cholinesterase inhibitors used in treatment of Alzheimer disease (Omran *et al.*, 2005). A number of donepezil analogues have been prepared with prospective in the treatment of Alzheimer disease (Andreani *et al.*, 2000). 1-Indanones are also important precursors in the regiospecific synthesis of 2-fluoro-1-naphthols (Cai *et al.*, 2005). 5-Chloro-1-indanone has been used to synthesize important biomedical compounds as anticonvulsants (Kwiecien *et al.*, 1991), anticholinergics (De Paulis *et al.*, 1981) and diarylsulphonylureas, which show great activity against solid tumours (Howbert *et al.*,1990).

The title compound, (I), was prepared as an intermediates for an isocoumarin synthesis and for the systematic study of its bioactivity. The synthesis was carried out by cyclodehydration of 3-(3,4,5-trimethoxyphenyl)propanoic acid using polyphosphoric acid.

A perspective view of (I) is shown in Fig. 1. Bond lengths and angles can be regarded as normal (Cambridge Crystallographic Database, Version 5.28, November 2006; Mogul Version 1.1; Allen, 2002, Bruno *et al.*, 2004). The atoms comprising the two rings are essentially planar (r.m.s. deviation for the nine C atoms 0.016 Å). Whereas one of the methoxy groups is almost coplanar with the aromatic ring, the other two are considerably twisted out of the plane of the aromatic ring (Table 1).

Experimental

3-(3,4,5-Trimethoxyphenyl)propanoic acid (1 g, 4.5 mmol) was dissolved in polyphosphoric acid (12.5 g) and the resulting yellow solution was heated along with stirring at 363 K for 2 h. The cooled solution was added to 200 ml ice water and extracted with ethyl acetate (4 × 100 ml). The combined extracts were washed with 5% sodium bicarbonate solution and then with water until the washings were neutral. The organic layer was dried ($MgSO_4$), filtered and rotary evaporated to dryness. Recrystallization from ethyl acetate afforded (I) as colorless crystals (0.758 g, 76%) m.p. 386 K; R_f 0.461 (Hexane-ethyl acetate 3:2 v/v); IR(cm^{-1}) 1685, 1590; ^{1}H NMR (400 MHz, C_6D_6O): δ 2.54 (m, 2H, H-3), 3.02 (m, 2H, H-2), 3.93 (s, 3H, OMe) 3.94 (s, 6H, OMe ×2), 6.89 (s, 1H, H-4); ^{13}C NMR (100 MHz, C_6D_6O): δ 25.26 (C-3), 36.7 (C-2),

55.73 (OMe) 66.4 (OMe), 61.16 (OMe), 104.29 (C-4), 122.68, 140.75, 151.38, 153.25, 159.66, 205 (CO); MS (70 eV): m/z (%) = 222 [M^+] (26), 194 (53), 180 (70), 179 (82). Anal. Calcd. For $C_{12}H_{14}O_4$: C 64.85, H 6.35; Found C 64.78, H 6.25.

Refinement

The H atoms were found in a difference map, relocated to idealised locations (C—H = 0.95-1.00 Å) and refined as riding with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(C_{methyl})$. The methyl groups were allowed to rotate but not to tip to best fit the electron density.

Figures

Fig. 1. Reaction scheme.

5,6,7-Trimethoxy-2,3-dihydroinden-1-one

Crystal data

$C_{12}H_{14}O_4$	$F_{000} = 472$
$M_r = 222.23$	$D_x = 1.351$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
Hall symbol: -P 2yn	Cell parameters from 10752 reflections
$a = 8.9319$ (7) Å	$\theta = 3.7–27.4°$
$b = 7.2870$ (5) Å	$\mu = 0.10$ mm^{-1}
$c = 16.8250$ (12) Å	$T = 173$ (2) K
$\beta = 94.070$ (6)°	Block, colourless
$V = 1092.32$ (14) Å^3	0.44 × 0.36 × 0.35 mm
$Z = 4$	

Data collection

Stoe IPDSII two-circle diffractometer	2228 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	$R_{int} = 0.037$
Monochromator: graphite	$\theta_{max} = 27.6°$
$T = 173(2)$ K	$\theta_{min} = 3.6°$
ω scans	$h = -11\rightarrow11$
Absorption correction: none	$k = -9\rightarrow9$
13559 measured reflections	$l = -21\rightarrow21$
2503 independent reflections	

Refinement

Refinement on F^2	H-atom parameters constrained
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0517P)^2 + 0.3007P]$ where $P = (F_o^2 + 2F_c^2)/3$

$R[F^2 > 2\sigma(F^2)] = 0.036$

$wR(F^2) = 0.099$

$S = 1.05$

2503 reflections

149 parameters

Primary atom site location: structure-invariant direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.31$ e Å^{-3}

$\Delta\rho_{min} = -0.18$ e Å^{-3}

Extinction correction: SHELXL97 (Sheldrick, 1997), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$

Extinction coefficient: 0.032 (3)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2$sigma(F^2) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.74306 (10)	0.18545 (11)	0.48369 (5)	0.0279 (2)
O2	0.69416 (9)	0.34326 (11)	0.62622 (5)	0.02385 (19)
O3	0.74311 (9)	0.70171 (11)	0.65236 (4)	0.0242 (2)
O4	0.86342 (11)	0.27959 (15)	0.32016 (5)	0.0386 (2)
C1	0.76746 (11)	0.37103 (14)	0.49242 (6)	0.0200 (2)
C2	0.74150 (11)	0.45090 (14)	0.56521 (6)	0.0190 (2)
C3	0.77195 (11)	0.64021 (14)	0.57867 (6)	0.0192 (2)
C4	0.82703 (11)	0.74926 (14)	0.51888 (6)	0.0211 (2)
H4	0.8468	0.8761	0.5275	0.025*
C5	0.85206 (11)	0.66692 (15)	0.44633 (6)	0.0210 (2)
C6	0.82389 (11)	0.48094 (15)	0.43221 (6)	0.0207 (2)
C7	0.86659 (12)	0.43158 (18)	0.35147 (6)	0.0268 (3)
C8	0.91705 (15)	0.6070 (2)	0.31223 (7)	0.0346 (3)
H8A	0.8481	0.6376	0.2654	0.042*
H8B	1.0195	0.5919	0.2943	0.042*
C9	0.91487 (13)	0.75968 (18)	0.37514 (7)	0.0294 (3)
H9A	1.0173	0.8070	0.3890	0.035*
H9B	0.8498	0.8626	0.3557	0.035*
C10	0.61698 (14)	0.13820 (18)	0.42970 (8)	0.0324 (3)
H10A	0.5251	0.1897	0.4492	0.049*
H10B	0.6079	0.0044	0.4263	0.049*

H10C	0.6320	0.1883	0.3768	0.049*
C11	0.53673 (13)	0.36075 (18)	0.63795 (8)	0.0310 (3)
H11A	0.5158	0.4856	0.6558	0.046*
H11B	0.5092	0.2726	0.6784	0.046*
H11C	0.4780	0.3360	0.5877	0.046*
C12	0.77570 (14)	0.89208 (16)	0.66966 (7)	0.0289 (3)
H12A	0.8829	0.9151	0.6653	0.043*
H12B	0.7494	0.9206	0.7239	0.043*
H12C	0.7169	0.9699	0.6316	0.043*

Atomic displacement parameters (Å^2)

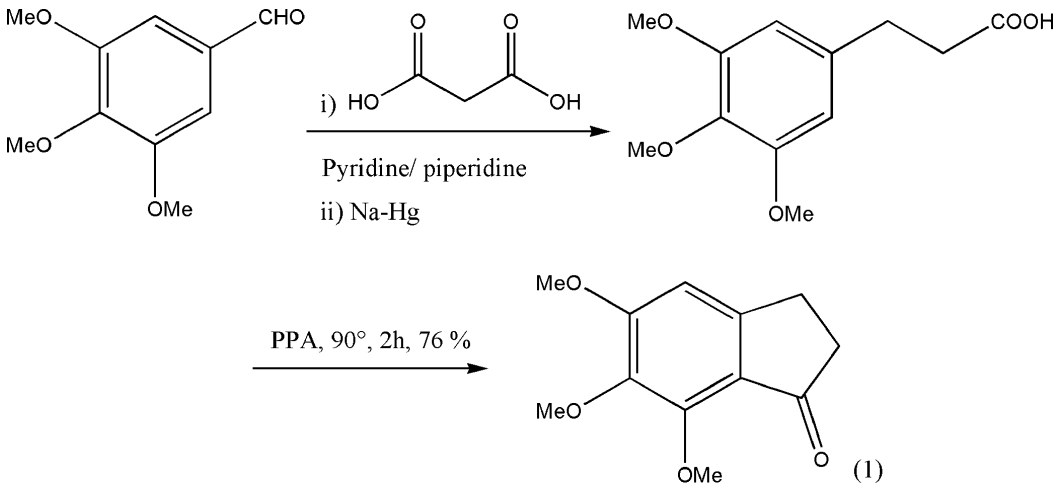
	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0334 (4)	0.0174 (4)	0.0317 (4)	0.0008 (3)	−0.0061 (3)	−0.0016 (3)
O2	0.0236 (4)	0.0224 (4)	0.0262 (4)	0.0001 (3)	0.0064 (3)	0.0081 (3)
O3	0.0298 (4)	0.0218 (4)	0.0216 (4)	−0.0020 (3)	0.0071 (3)	−0.0021 (3)
O4	0.0362 (5)	0.0486 (6)	0.0316 (5)	0.0022 (4)	0.0063 (4)	−0.0149 (4)
C1	0.0185 (5)	0.0176 (5)	0.0235 (5)	0.0025 (4)	−0.0015 (4)	0.0009 (4)
C2	0.0169 (5)	0.0191 (5)	0.0209 (5)	0.0007 (4)	0.0022 (4)	0.0043 (4)
C3	0.0174 (5)	0.0207 (5)	0.0197 (5)	0.0016 (4)	0.0020 (4)	0.0008 (4)
C4	0.0204 (5)	0.0186 (5)	0.0246 (5)	−0.0001 (4)	0.0026 (4)	0.0032 (4)
C5	0.0163 (4)	0.0252 (5)	0.0216 (5)	0.0022 (4)	0.0019 (4)	0.0059 (4)
C6	0.0170 (5)	0.0259 (5)	0.0190 (5)	0.0041 (4)	0.0001 (4)	0.0010 (4)
C7	0.0185 (5)	0.0409 (7)	0.0208 (5)	0.0058 (4)	0.0005 (4)	−0.0020 (5)
C8	0.0313 (6)	0.0515 (8)	0.0218 (5)	0.0026 (6)	0.0069 (4)	0.0061 (5)
C9	0.0270 (6)	0.0349 (6)	0.0271 (6)	0.0030 (5)	0.0076 (4)	0.0120 (5)
C10	0.0315 (6)	0.0287 (6)	0.0363 (6)	−0.0045 (5)	−0.0026 (5)	−0.0055 (5)
C11	0.0244 (6)	0.0339 (6)	0.0357 (6)	−0.0051 (5)	0.0095 (5)	0.0039 (5)
C12	0.0348 (6)	0.0235 (6)	0.0290 (6)	−0.0027 (5)	0.0051 (4)	−0.0064 (4)

Geometric parameters (Å, °)

O1—C1	1.3760 (13)	C7—C8	1.5217 (18)
O1—C10	1.4377 (14)	C8—C9	1.5366 (19)
O2—C2	1.3818 (12)	C8—H8A	0.9900
O2—C11	1.4394 (13)	C8—H8B	0.9900
O3—C3	1.3600 (12)	C9—H9A	0.9900
O3—C12	1.4429 (14)	C9—H9B	0.9900
O4—C7	1.2259 (16)	C10—H10A	0.9800
C1—C2	1.3901 (14)	C10—H10B	0.9800
C1—C6	1.4122 (15)	C10—H10C	0.9800
C2—C3	1.4211 (15)	C11—H11A	0.9800
C3—C4	1.3984 (14)	C11—H11B	0.9800
C4—C5	1.3924 (15)	C11—H11C	0.9800
C4—H4	0.9500	C12—H12A	0.9800
C5—C6	1.3957 (16)	C12—H12B	0.9800
C5—C9	1.5171 (14)	C12—H12C	0.9800
C6—C7	1.4810 (14)		

C1—O1—C10	114.45 (9)	C7—C8—H8B	110.3
C2—O2—C11	113.90 (8)	C9—C8—H8B	110.3
C3—O3—C12	116.89 (8)	H8A—C8—H8B	108.6
O1—C1—C2	118.07 (9)	C5—C9—C8	104.16 (10)
O1—C1—C6	122.86 (10)	C5—C9—H9A	110.9
C2—C1—C6	119.01 (10)	C8—C9—H9A	110.9
O2—C2—C1	119.72 (9)	C5—C9—H9B	110.9
O2—C2—C3	119.85 (9)	C8—C9—H9B	110.9
C1—C2—C3	120.32 (9)	H9A—C9—H9B	108.9
O3—C3—C4	124.58 (10)	O1—C10—H10A	109.5
O3—C3—C2	114.75 (9)	O1—C10—H10B	109.5
C4—C3—C2	120.67 (9)	H10A—C10—H10B	109.5
C5—C4—C3	118.18 (10)	O1—C10—H10C	109.5
C5—C4—H4	120.9	H10A—C10—H10C	109.5
C3—C4—H4	120.9	H10B—C10—H10C	109.5
C4—C5—C6	121.97 (9)	O2—C11—H11A	109.5
C4—C5—C9	126.26 (10)	O2—C11—H11B	109.5
C6—C5—C9	111.75 (10)	H11A—C11—H11B	109.5
C5—C6—C1	119.85 (9)	O2—C11—H11C	109.5
C5—C6—C7	109.69 (10)	H11A—C11—H11C	109.5
C1—C6—C7	130.43 (10)	H11B—C11—H11C	109.5
O4—C7—C6	127.87 (11)	O3—C12—H12A	109.5
O4—C7—C8	124.83 (11)	O3—C12—H12B	109.5
C6—C7—C8	107.30 (10)	H12A—C12—H12B	109.5
C7—C8—C9	106.90 (9)	O3—C12—H12C	109.5
C7—C8—H8A	110.3	H12A—C12—H12C	109.5
C9—C8—H8A	110.3	H12B—C12—H12C	109.5
C10—O1—C1—C2	111.17 (11)	C4—C5—C6—C1	0.38 (15)
C10—O1—C1—C6	−71.82 (13)	C9—C5—C6—C1	178.89 (9)
C11—O2—C2—C1	−103.31 (11)	C4—C5—C6—C7	−177.77 (9)
C11—O2—C2—C3	80.44 (12)	C9—C5—C6—C7	0.73 (12)
O1—C1—C2—O2	0.67 (14)	O1—C1—C6—C5	−177.24 (9)
C6—C1—C2—O2	−176.46 (9)	C2—C1—C6—C5	−0.25 (15)
O1—C1—C2—C3	176.91 (9)	O1—C1—C6—C7	0.48 (17)
C6—C1—C2—C3	−0.22 (15)	C2—C1—C6—C7	177.47 (10)
C12—O3—C3—C4	−1.56 (15)	C5—C6—C7—O4	176.68 (11)
C12—O3—C3—C2	178.52 (9)	C1—C6—C7—O4	−1.22 (19)
O2—C2—C3—O3	−3.26 (13)	C5—C6—C7—C8	−3.29 (12)
C1—C2—C3—O3	−179.49 (9)	C1—C6—C7—C8	178.82 (10)
O2—C2—C3—C4	176.82 (9)	O4—C7—C8—C9	−175.48 (11)
C1—C2—C3—C4	0.59 (15)	C6—C7—C8—C9	4.49 (12)
O3—C3—C4—C5	179.63 (9)	C4—C5—C9—C8	−179.50 (10)
C2—C3—C4—C5	−0.46 (15)	C6—C5—C9—C8	2.07 (12)
C3—C4—C5—C6	−0.02 (15)	C7—C8—C9—C5	−3.94 (12)
C3—C4—C5—C9	−178.30 (10)		

Fig. 1


MeO
CHO
MeO
OMe
i) HO
OH
Pyridine/ piperidine
ii) Na-Hg
MeO
COOH
MeO
OMe
PPA, 90°, 2h, 76 %
MeO
MeO
OMe
O

(1)